JC10 Rec'd PCT/PTO 08 MAR 2002

Form PTO-1390 (Rev. 12-29-99) US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NO. **H 4304 PCT/US** U.S. APPLICATION NO. (if known see 37 CFR 1.5) **10/070590**
INTERNATIONAL APPLICATION NO. **PCT/EP00/08435**	INTERNATIONAL FILING DATE **August 30, 2000**	PRIORITY DATE CLAIMED **September 8, 1999**

TITLE OF INVENTION
SUNSCREEN AGENT FOR ORAL ADMINISTRATION

APPLICANT(S) FOR DO/EO/US
Christine Gaertner, Wilhelm Stahl, Ulrike Heinrich

Applicant herewith submits to the United States Designated/Elected Office (EO/DO/US) the following items and other information:

1. ■ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. □ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. □ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39 (1).
4. ■ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ■ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. □ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. □ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ■ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. □ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. □ have been transmitted by the International Bureau.
   c. □ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ■ have not been made and will not be made.
8. □ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ■ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). **(UNEXECUTED)**
10. □ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. □ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. □ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ■ A FIRST preliminary amendment
    □ A SECOND or SUBSEQUENT preliminary amendment.
14. □ A substitute specification.
15. □ A change of power of attorney and/or address letter.
16. □ Other items or information:

"Express Mail Post Office to Addressee" service Mailing Label Number EL541614355US .

JC13 Rec'd PCT/PTO 08 MAR 2002

U.S. Application No. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/070590	PCT/EP00/08435	H 4304 PCT/US

17. ■ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO.....**$1,040.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO.....**$890.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37CFR 1.445(a)(2)) paid to USPTO **$740.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**

International preliminary examination fee paid to USPTO (37CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4).....**$100.00**

	CALCULATIONS	PTO USE ONLY
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date 37 (CFR 1.492(e)).	$ 0	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	10 - 20 =	0	0 X $18.00	$ 0	
Independent Claims	2 - 3 =	0	0 X $84.00	$ 0	
Multiple dependent claims (s)(if applicable)		0	+ $280.00	$ 0	
TOTAL OF ABOVE CALCULATIONS =				$ 890	
Reduction of ½ for filing by small entity, if applicable. A Small Entity Statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ 0	
SUBTOTAL =				$ 890	
Processing fee of **$130.00** for furnishing the English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$ 0	
TOTAL NATIONAL FEE =				$ 890	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +				$ 0	
TOTAL FEES ENCLOSED =				$ 890	
				Amount to be: refunded:	$----------
				charged:	$890.00

a. ☐ A check in the amount of $_____ to cover the above fees is enclosed.

b. ■ Please charge my Deposit Account No. 50-1177 in the amount of $890.00 to cover the above fees. A triplicate copy of this sheet is enclosed. Order No. 02-0112 .

c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1177 . A triplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO: **Customer Label No. 23657**

SIGNATURE

Aaron R. Ettelman
NAME ATTORNEY FOR APPLICANT

42,516
REGISTRATION NUMBER

"Express Mail " Mailing Label Number EL541614355US .

PATENT
Docket No. H 4304 PCT/US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RE: PCT/EP00/08435
International Filing Date: August 30, 2000
Priority Date Claimed: September 8, 1999
Applicant: Gaertner, et al.
Title: SUNSCREEN AGENT FOR ORAL ADMINISTRATION
Applicants' Reference: H 4304 PCT/US

PRELIMINARY AMENDMENT

Commissioner for Patents
Box PCT
Washington, DC 20231

ATTN: DO/EO/US

Prior to the calculation of fees and examination of the above-identified national stage application pursuant to the accompanying submission under 35 U.S.C. §371, please amend the English translation of the International Application submitted herewith, without prejudice, as follows:

In the Specification:

Please amend the instant Specification, without prejudice, as follows:

Please delete all text above line 7 of page 1, including the heading "Prior Art", and replace the deleted matter with the following new section headings and title of the invention:

--TITLE OF THE INVENTION

Oral Administration of β-Carotene, Lycopene and Lutein for Human Skin Protection

BACKGROUND OF THE INVENTION--

At page 3, line 18 thereof, please delete the section heading "Description of the Invention" and insert the following new section heading and new paragraph:

Preliminary Amendment of U.S. National Stage for International Application PCT/EP00/08435 filed August 30, 2000

--BRIEF SUMMARY OF THE INVENTION

The present invention relates, in general, to orally administered sun protection preparations and more particularly to a mixture of β-carotene, lutein and lycopene.--

At page 4, line 6 thereof, please insert the following new section heading:

--DETAILED DESCRIPTION OF THE INVENTION--

At page 12, between lines 1 and 2, please add the following new paragraph: --What is claimed is:--.

On a separate, new page 14, please add the following new section heading and paragraph containing an Abstract of the Disclosure:

--ABSTRACT OF THE DISCLOSURE

Methods of improving the sun protection factor of human skin and methods of inhibiting the aging of human skin via the oral administration of a composition comprising (a) β-carotene, (b) lutein and (c) lycopene, in a ratio by weight (a):(b):(c) of from 1:0.5:0.5 to 1:1.5:1.5 are described.--

In the Claims:

Please add new claims 8-17, as follows:

--8. (New) A method of improving the sun protection factor of human skin, the method comprising:

(i) providing a composition comprising (a) β-carotene, (b) lutein and (c) lycopene, in a ratio by weight (a):(b):(c) of from 1:0.5:0.5 to 1:1.5:1.5; and

(ii) orally administering the composition to a human.--

--9. (New) The method according to claim 8, wherein the composition further comprises one or more components selected from the group consisting of α-carotene, astaxanthin, α-cryptoxanthin, β-cryptoxanthin, zeaxanthin, phytoene, phtyofluene, γ-carotene and neurosporin.--

--10. (New) The method according to claim 8, wherein the β-carotene, the lutein and the lycopene in a ratio by weight of from 1:0.5:0.5 to 1:1.0:1.0.--

--11. (New) The method according to claim 8, wherein the composition is dispersed in an edible oil.--

--12. (New) The method according to claim 8, wherein the β-carotene, the lutein and the lycopene are each present in an amount of from 1 to 40 mg.--

--13. (New) A method of inhibiting the aging of human skin, the method comprising:

(i) providing a composition comprising (a) β-carotene, (b) lutein and (c) lycopene, in a ratio by weight (a):(b):(c) of from 1:0.5:0.5 to 1:1.5:1.5; and

(ii) orally administering the composition to a human.--

--14. (New) The method according to claim 13, wherein the composition further comprises one or more components selected from the group consisting of α-carotene, astaxanthin, α-cryptoxanthin, β-cryptoxanthin, zeaxanthin, phytoene, phtyofluene, γ-carotene and neurosporin.--

--15. (New) The method according to claim 13, wherein the β-carotene, the lutein and the lycopene in a ratio by weight of from 1:0.5:0.5 to 1:1.0:1.0.--

Preliminary Amendment of U.S. National Stage for International Application PCT/EP00/08435 filed August 30, 2000

--16. (New) The method according to claim 13, wherein the composition is dispersed in an edible oil.--

--17. (New) The method according to claim 13, wherein the β-carotene, the lutein and the lycopene are each present in an amount of from 1 to 40 mg.--

Please cancel claims 1-7, without prejudice.

Preliminary Amendment of U.S. National Stage for International Application PCT/EP00/08435 filed August 30, 2000

REMARKS

Claims 8-17 are currently pending in the instant application.

The Specification has been amended to delete the original section headings and to insert the preferred section headings pursuant to 37 C.F.R. §1.77. A new Title of the Invention has been inserted. An Abstract of the Disclosure, in accordance with the disclosure, has been added. It is submitted that the amendments to the Specification made herein introduce no new matter. All of the amendments to the Specification constitute deletions of original section headings and/or paragraphs, and insertions or additions of new section headings and/or paragraphs. Accordingly, pursuant to 37 C.F.R. §1.121(b)(1)(iii), no separate page captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" is necessary. A separate page containing a clean copy of the Abstract of the Disclosure has been attached for the Examiner's convenience. Entry of the amendments to the Specification made herein are therefore proper and respectfully requested.

Original claims 1-7 have been canceled and replaced with new claims 8-17 solely for the purpose of improving clarity and grammar, which may suffer in translation, and not for any reason which relates to the statutory requirements for a patent. New claims 8-17 have not been added in response to any rejection, nor in anticipation of any rejection. Applicants respectfully submit that the scope of new claims 8-17 generally corresponds to the scope of original claims 1-7, and that new claims 8-17 are no narrower than original claims 1-7. Furthermore, although a moot point in view of their cancellation, Applicants respectfully submit that original claims 1-7 satisfied the requirements of 35 U.S.C. §112, as filed. New claims 8-17 are supported by the claims as originally filed and in the Specification, for example, at page 3, line 19, through page 4, line 3; at page 6, lines 10-17; and in the Examples. No new matter has been introduced. All of the amendments to the Claims constitute cancellation of original claims and the addition of new claims. Accordingly, pursuant to 37 C.F.R. §1.121(c)(1)(ii), no separate page captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" is necessary. Entry is therefore proper and respectfully requested.

Preliminary Amendment of U.S. National Stage for International Application PCT/EP00/08435 filed August 30, 2000

Prompt examination of the instant application in view of the amendments made herein is respectfully requested.

Respectfully submitted,

CHRISTINE GAERTNER, *et al.*

March 8, 2002
(Date)

AARON R. ETTELMAN
(Reg. No. 42,516)
Attorney for Applicants
Telephone: (610) 278-4930
Facsimile: (610) 278-4971
E-Mail: AARON.ETTELMAN@HENKEL-AMERICAS.COM

Cognis Corporation, Patent Dept.
2500 Renaissance Blvd., Suite 200
Gulph Mills, PA 19406

ARE/ras

G:\Data\amend\H4304.pam.doc

ABSTRACT OF THE DISCLOSURE

Methods of improving the sun protection factor of human skin and methods of inhibiting the aging of human skin via the oral administration of a composition comprising (a) β-carotene, (b) lutein and (c) lycopene, in a ratio by weight (a):(b):(c) of from 1:0.5:0.5 to 1:1.5:1.5 are described.

Sunscreen Agent for Oral Administration

Field of the Invention

This invention relates generally to orally administered sun protection preparations and more particularly to a mixture of β-carotene, lutein and lycopene.

Prior Art

Under the influence of the sun's rays, normal skin is pigmented by the formation of melanin. Exposure to long-wave UV-A light results in darkening of the melanins already present in the epidermis without any harmful effects while exposure to short-wave UV-B radiation results in the formation of new melanin. However, before the protective pigment can be formed, the skin is exposed to the effect of unfiltered radiation which can lead to reddening of the skin (erythema), inflammation of the skin (sunburn) or even to blisters, depending on the exposure time. The strain on the organism associated with such skin lesions, for example in connection with the distribution of histamines, can additionally lead to headache, lassitude, fever, heart and circulation problems and the like. In addition, long-term exposure can lead to cumulative DNA damage which can result in skin cancer. Consumers seeking to protect themselves against the harmful effects of the sun basically have two choices: first, they can protect the skin by topical application of cosmetic preparations containing UV protection factors, second they can increase the skin's own protection factor by oral application of suitable compounds.

European patent application **EP 0 712 630 A2** (JBC Cosmetics) describes an orally administered preparation containing a carotinoid, a tocopherol, ascorbic acid and selenium. This preparation is intended to tan the skin and to prevent sun allergies (photodermatoses). α-Carotene, β-

carotene and lycopene are used as the carotinoids in daily doses of 60 to 150 mg.

French patent application **FR 2 698 268 A1** (L'Oréal) describes a composition for oral administration to human beings which contains tyrosine and/or phenyl alanine, a copper salt and a mixture of vitamins. Carotenes, vitamin E, niacin and vitamin C may be used as the vitamins. The carotenes mentioned include α-, β- and γ-carotene and lycopene which may be used in doses of 5 to 50 mg. The preparation is intended to protect the skin against the harmful effects of UV radiation.

Sun protection preparations for topical application where synthetic UV filters are replaced by substances of natural origin are described in **EP 0 747 039 A2** (SA.FO.SA.). These sun protection preparations contain a mixture of amino acids, vitamins and/or provitamins, nucleoderivatives and vegetable extracts and may be used in the form of gels, creams or oils.

International patent application **WO 97/47278** (Laboratoires Oenobiol.) claims a mixture for oral application containing

(a) at least one natural carotinoid with provitamin A character (either α- or β-carotene),

(b) at least one natural carotinoid without provitamin A character (lycopene) and

(c) another carotinoid selected from the group consisting of zeaxanthin, cryptoxanthin and lutein,

the ratio of (a) to (b) being 0.95:1 to 1:50. In Example 1, this application describes a composition of 2.86 mg β-carotene and 3 mg lycopene. The mixture also contains 0.07 mg lutein as a secondary component of the β-carotene source.

Accordingly, the prior art literature describes numerous oral preparations which are supposed to increase the skin's own sun protection factor. Most of these preparations are based on α- or β-carotene. Since studies have shown that the supplementation of β-carotene can increase

the incidence of lung cancer (**ATBC Study**, The New England Journal of Medicine, 1994, 330, 1029-1035 and **CARET Study**, G.S. Omenn et al., The New England Journal of Medicine, 1996, 334, 1150-1155), there is a need for a substitute or partial substitute for β-carotene in known oral sun protection preparations.

Accordingly, the problem addressed by the present invention was to provide improved sun protection preparations for oral administration. More particularly, by comparison with known sun protection preparations, a proportion of α- or β-carotene would be replaced by other, at least equally effective substances. The requirements which these substitutes would be expected to satisfy would be stringent. Besides providing comparable or better protection against the sun, they would have to be toxicologically safe and easy to handle and formulate. In addition, the substitutes in question would preferably be substances of natural origin. Besides increasing the skin's own sun protection factor, the sun protection preparations provided by the invention would also delay ageing of the skin.

Description of the Invention

The present invention relates to orally administered preparations containing

(a) β-carotene,

(b) lutein and

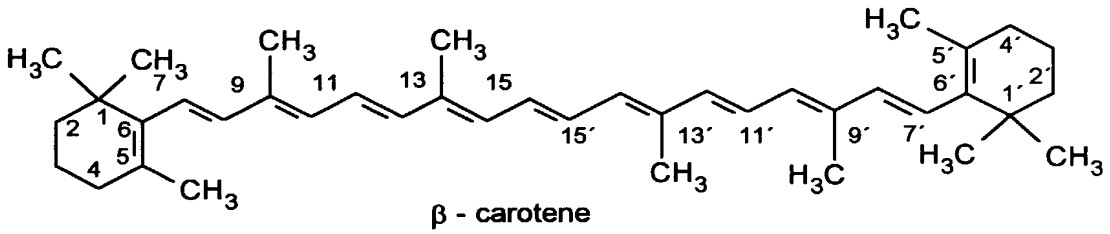
(c) lycopene

in a ratio by weight of (a) to (b) to (c) of 1 : (0.5 - 1.5) : (0.5 - 1.5) in a carrier suitable for oral administration.

It has surprisingly been found that the oral administration of the preparations according to the invention increases the sun protection factor of the skin and at the same time delays ageing of the skin. The mixtures are toxicologically safe for oral administration and are easy to formulate. It has surprisingly been found that the mixture of these three particular

carotinoids in the claimed ratio to one another is particularly suitable for increasing the sun protection factor of the skin and for delaying the ageing process of the skin. In contrast to the mixtures of WO 97/47278, the mixtures according to the invention produce a distinctly improved increase in the sun protection factor of the skin.

β-Carotene

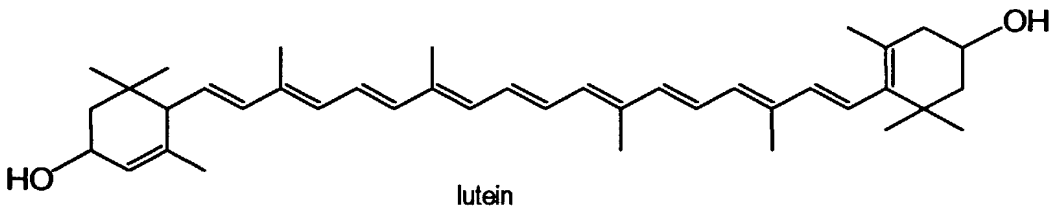


β - carotene

β-Carotene is an 11x-unsaturated tetraterpene. The chemical skeleton consists of nine conjugated double bonds and two β-ionone ring structures at the ends of the molecule where the double bonds of the β-ionone system are in conjugation with the unsaturated system of the polyene chain. The double bonds may be in the trans position (trans-β-carotene, β,β-carotene, provitamin A) or in the cis position (for example 9-cis-β-carotene and 13-cis-β-carotene). β-carotene in the context of the invention encompasses both the cis and the trans isomers of β-carotene. The β-carotene may be obtained both by extraction from vegetable sources (for example carrots and other vegetables, palm oil) or from animal materials, bacteria and/or algae (more particularly from the alga Dunaliella salina) and microbiologically or synthetically via vitamin A (retinol). It is particularly preferred to use β-carotene obtained by extraction from algae, more particularly by extraction from the alga Dunaliella salina which is commercially obtainable as Betatene®.

Lutein

Lutein in the context of the present invention includes both lutein itself [=(3R,3'R,6'R)-β,ε-carotene-3,3'-diol; $C_{40}H_{56}O_2$; MW 568.85] and the fatty acid esters of lutein. Suitable fatty acid esters are the esters of palmitic acid, myristic acid, stearic acid, lauric acid and oleic acid, the esters being both mono- and diesters and mixed forms (for example lutein myristyl palmitate).



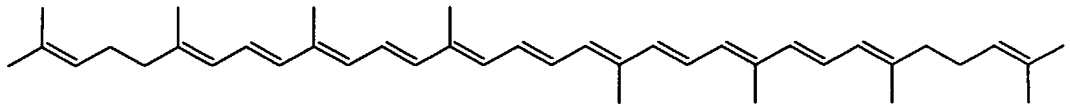
lutein

Lutein and its fatty acid esters may be obtained both by extraction from vegetable material (for example from varieties of Tagetes erecta (grass-of-Parnassus), stinging nettle leaves, lucern (for example alfalfa), palm oil), by extraction from animal material (for example egg yolk) and from bacteria or algae. It is particularly preferred to use lutein obtained by extraction from plants, more particularly lutein obtained by extraction from Tagetes erecta varieties which is commercially available as Xangold®.

Lycopene

Lycopene in the context of the present invention includes both the all trans isomer (ψ,ψ-carotene, $C_{40}H_{56}$, MW 536.85) and the cis isomers (such as, for example, 5-cis-, 9-cis-, 13-cis- and 15-cis-lycopene). Lycopene can be obtained by extraction from plants (tomato (Solanum lycopersicum), rose hip and other fruits, chanterelles (Cantharellus cibarius)) and by extraction from animal material. Lycopene can also be obtained by synthesis or extraction from microorganisms (fermentative protection). It is

particularly preferred to use lycopene obtained by fermentation or by extraction from plants.



lycopene

The ratio of the individual components to one another is crucial to the invention. It has surprisingly been found that, where components (a), (b) and (c) are present in a ratio of (a) to (b) to (c) of 1 : (0.5-1.5) : (0.5-1.5), the preparations obtained are distinguished from known preparations by a particularly effective increase in the sun protection factor of the skin. Particularly preferred preparations are those with a ratio of (a) to (b) to (c) of 1 : (0.5 - 1.0) : (0.5 - 1.0), more particularly 1.0 : 1.0: 1.0, and a ratio of 1 : 0.5 : 0.5 and 1: 0.75 : 0.75.

Carriers suitable for oral application

A key component of the preparations according to the invention is the carrier suitable for oral application. It is intended on the one hand to dissolve or disperse the carotinoid mixture according to the invention. In addition, it preferably supports the absorption of the carotinoids from the gastrointestinal tract. In principle, suitable carriers are any substances which perform these functions and which are toxicologically safe. Examples of suitable carriers are edible oils (particularly soybean oil), such as vegetable and fish oils which may optionally be partly hydrogenated, and carriers based on animal products, for example gelatine. Other suitable carrier materials are, for example, gum arabic, sucrose, lipids, mono- and diglycerides and maltodextrins. Where water is used as the carrier material, it is standard practice to use a suitable emulsifier (for example lecithins, sorbitan monolaurate).

The preparations may be orally administered, for example, as solutions, oils, emulsions, suspensions or dispersions. Suitable carrier forms are, for example, capsules or tablets. The preparations according to the invention are normally present in the form of soft gelatine capsules.

The preparations according to the invention are normally prepared by preparing a mixture of β-carotene, lutein and lycopene and then encapsulating the mixture thus prepared together with the carrier material.

The present invention includes the observation that the preparations according to the invention may be added to foods and that the foods thus enriched may be used as carriers for oral administration.

The present invention also includes the observation that typical antioxidants such as, for example, ascorbyl palmitate (E 304), mixed tocopherols (E 306), citric acid (E 330) or L-ascorbic acid (E 300) may be added to the preparations according to the invention.

In a preferred embodiment of the invention, the preparations according to the invention contain at least one other substance selected from the group consisting of α-carotene, astaxanthin, α-cryptoxanthin, β-cryptoxanthin, zeaxanthin, phytoene, phytofluene, γ-carotene and neurosporin.

The systematic names of the substances mentioned are as follows:

α-carotene	β,ε-carotene
astaxanthin	(3S,3'S)-3,3'-dihydroxy-β,β-carotene-4,4'-dione
α-cryptoxanthin	(3R)-β,ε-carotene-3-ol
β-cryptoxanthin	(3R)-β,β-carotene-3-ol
zeaxanthin	(3R,3'R)-β,β-carotene-3,3'-diol)
phytoene	7,8,11,12,7',8',11',12'-octahydro-ψ,ψ-carotene
phytofluene	7,8,11,12,7',8'-hexahydro-ψ,ψ-carotene
γ-carotene	β,ψ-carotene
neurosporin	7,8-ψ,ψ-carotene.

It is particularly preferred to use α-carotene.

It has surprisingly been found that the sun protection factor of the skin is increased by the oral administration of preparations containing (a) β-carotene, (b) lutein and (c) lycopene in a ratio by weight of (a) to (b) to (c) of 1 : (0.5 - 1.5) : (0.5 - 1.5) in a carrier suitable for oral administration. Accordingly, the present invention also relates to a process for increasing the sun protection factor of human skin, characterized in that the preparations according to the invention are orally administered.

The sun protection factor of the skin may be determined by any of the methods known to the expert such as, for example, determination of the minimum erythema activity (MED) as described by COLIPA. Other methods include determination of the melanin content and the concentration of the carotinoids in the skin by reflection spectrophotometry and/or HPLC and chromometric determination of skin color (a, b and L values). A description of these methods can be found, for example, in **Biochemistry and Molecular Biology International, 42, No. 5, 1997, pp. 1023-1033**.

The duration of supplementation is normally determined by the existing sun protection factor of the skin and by the - individually very different - absorption capacity. It may be carried out for several days, several weeks or even for several months or years. Because the preparations according to the invention are toxicologically safe, supplementation may even be carried out indefinitely, as desirable for example in people exposed much more than normal UV radiation.

It has surprisingly been found that the ageing process of human skin is delayed by the oral administration of preparations containing (a), (b) and (c) in a ratio by weight of 1 : (0.5 - 1.5) : (0.5 - 1.5) in a carrier suitable for oral administration. Accordingly, the present invention also relates to a process for delaying the ageing process of the skin, characterized in that the preparations according to the invention are orally administered.

The duration of supplementation is normally determined by the state of ageing of the skin and by the - individually very different - absorption capacity. It may be carried out for several days, several weeks or even for several months or years. Because the preparations according to the invention are toxicologically safe, supplementation may even be carried out indefinitely.

The quantity of components (a), (b) and (c) - expressed as a daily dose - is normally between 1 and 40 mg per component, with the proviso that the ratio of (a) to (b) to (c) is 1 : (0.5 - 1.5) : (0.5 - 1.5). Quantities of 2 to 25 mg per component and more particularly 5 to 10 mg per component are preferred. The preparations according to the invention may be administered as a single daily dose or as several doses distributed over a day.

The present invention also relates to the use of the orally administered preparations claimed in claim 1 for increasing the sun protection factor of human skin.

The present invention also relates to the use of the orally administered preparations claimed in claim 1 for delaying the ageing process of human skin.

Examples

The carotinoid absorption and photoprotection studies were carried out using a panel of 36 volunteers with healthy skin of light type II (Fitzpatrick & Pathak test). The starting values for each volunteer were determined at the beginning of the 12-week study. An interim study was conducted after 6 weeks and the final study after 12 weeks. The volunteers were divided into three groups of twelve who received the following daily doses:

1st group: 25 mg Betatene® (corresponds to 24 mg β-carotene)

2nd group: 8.3 mg Betatene® (corresponds to 8 mg β-carotene), 8 mg lycopene, 8 mg lutein (Xangold®)

3rd group: placebo capsules.

The carotinoids were administered in soft gelatine capsules with 140 mg soybean oil.

The concentration of β-carotene, lycopene and lutein in the skin was determined by reflection spectrometry which was carried out on an area of 1 cm^2 of the forehead, the back of the hand, the palm of the hand, the inside of the lower arm and the back. The change in color of the skin during supplementation was differentiated by a Minolta chromameter (L, a, b system) into reddening of the skin (a values), yellow component (b values) and lightness of the skin (L values). The concentration of β-carotene, lycopene and lutein in the serum was determined by high-pressure liquid chromatography (HPLC).

The results are set out in Table 1 and represent the average values for the volunteer panel on completion of the study. The photoprotective value is expressed relative to the blank value (i.e. no addition of carotinoids, group 3).

Table 1

Photoprotective effect

Group	Carotinoids (daily dose)	Photoprotection [%-rel.]
1	β-carotene (24 mg)	200
2	β-carotene (8 mg), lycopene (8 mg) and lutein (8 mg)	270
3	Control group with no carotinoids	100

It can be seen that the administration of the Betatene mixture (β-carotene) doubles the photoprotection of the skin (group 2) in relation to the blank value (group 3). Where mixtures of Betatene (β-carotene) and lutein and lycopene are used, a distinct increase in photoprotection is obtained (group 2). The group 2 results clearly show that this effect is not an additive one because the same quantity of β-carotene (group 3) fails to achieve this protective effect.

CLAIMS

1. Orally administered preparations containing

(a) β-carotene,

(b) lutein and

(c) lycopene

in a ratio by weight of (a) to (b) to (c) of 1 : (0.5 - 1.5) : (0.5 - 1.5) in a carrier suitable for oral administration.

2. Preparations as claimed in claim 1, characterized in that they contain at least one other substance selected from the group consisting of α-carotene, astaxanthin, α-cryptoxanthin, β-cryptoxanthin, zeaxanthin, phytoene, phytofluene, γ-carotene and neurosporin.

3. A process for increasing the sun protection factor of human skin, characterized in that preparations containing

(a) β-carotene,

(b) lutein and

(c) lycopene

in a ratio by weight of (a) to (b) to (c) of 1 : (0.5 - 1.5) : (0.5 - 1.5) are orally administered to the human body in a carrier suitable for oral administration.

4. A process for delaying the ageing process of human skin, characterized in that preparations containing

(a) β-carotene,

(b) lutein and

(c) lycopene

in a ratio by weight of (a) to (b) to (c) of 1 : (0.5 - 1.5) : (0.5 - 1.5) are orally administered to the human body in a carrier suitable for oral administration.

5. A process as claimed in claims 3 and/or 4, characterized in that the preparations contain

1 to 40 mg (a) β-carotene,

1 to 40 mg (b) lutein and

1 to 40 mg (c) lycopene

as a daily dose, with the proviso that the ratio of (a) to (b) to (c) is 1 : (0.5 - 1.5) : (0.5 - 1.5).

6. The use of the orally administered preparations claimed in claim 1 for oral administration for increasing the sun protection factor of the skin.

7. The use of the orally administered preparations claimed in claim 1 for delaying the ageing process of the skin.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

(43) Internationales Veröffentlichungsdatum
15. März 2001 (15.03.2001)

PCT

(10) Internationale Veröffentlichungsnummer
WO 01/17519 A1

(51) Internationale Patentklassifikation[7]: A61K 31/07, A61P 39/06, 17/16

(21) Internationales Aktenzeichen: PCT/EP00/08435

(22) Internationales Anmeldedatum:
30. August 2000 (30.08.2000)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
199 42 774.7 8. September 1999 (08.09.1999) DE

(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: **COGNIS DEUTSCHLAND GMBH** [DE/DE]; Henkelstr. 67, 40589 Düsseldorf (DE).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: **GÄRTNER, Christine** [DE/DE]; Gotenstrasse 3, 40225 Düsseldorf (DE). **STAHL, Wilhelm** [DE/DE]; Luegallee 6, 40545 Düsseldorf (DE). **HEINRICH, Ulrike** [DE/DE]; Altarhof 6, 58300 Wetter (DE).

(81) Bestimmungsstaaten *(national)*: AU, JP, US.

(84) Bestimmungsstaaten *(regional)*: europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Veröffentlicht:
— *Mit internationalem Recherchenbericht.*
— *Vor Ablauf der für Änderungen der Ansprüche geltenden Frist; Veröffentlichung wird wiederholt, falls Änderungen eintreffen.*

Zur Erklärung der Zweibuchstaben-Codes, und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen

WO 01/17519 A1

(54) **Title:** SUNSCREEN AGENT FOR ORAL ADMINISTRATION

(54) **Bezeichnung:** SONNENSCHUTZMITTEL ZUR ORALEN AUFNAHME

(57) **Abstract:** The invention relates to preparations for oral administration, comprising a defined ratio of β-carotene, lutein and lycopine . The invention also relates to methods for increasing the light protection factor of the skin and delaying the ageing process of the skin, in addition to the use of said preparations.

(57) **Zusammenfassung:** Vorgeschlagen werden Zubereitungen zur oralen Aufnahme, die β-Carotin, Lutein und Lycopin einem definierten Verhältnis zueinander enthalten, Verfahren zur Erhöhung des Lichtschutzfaktors der Haut sowie zur Verzögerung des Alterungsprozesses der Haut sowie die Verwendung dieser Zubereitungen.

"Express Mail" mailing label number EL541614355US .

PTO/SB/01 (6-95)
Approved for use through: 10/31/98 OMB 0651-0032
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Type a plus sign (+) inside this box → ☐

0010/PTO
Rev. 6/95

U.S. Department of Commerce
Patent and Trademark Office

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

☐ Declaration Submitted with Initial Filing OR ☒ Declaration Submitted after Initial Filing

Attorney Docket Number	H 4304 PCT/US
First Named Inventor	GAERTNER, Christine
COMPLETE IF KNOWN	
Application Number	10/070,590
Filing Date	07/30/2002
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:
My residence, post office address, and citizenship are as stated below next to my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

SUNSCREEN AGENT FOR ORAL ADMINISTRATION

(Title of the Invention)

the specification of which
☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY) 08/30/2000 as United States Application Number or PCT International Application Number PCT/EP00/08435 and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY	Priority Not Claimed	Certified Copy Attached? YES	Certified Copy Attached? NO
199 42 774.7	DE	09/08/1999	☐	☐	☒

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

Burden Hour Statement: This form is estimated to take .4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

"Express Mail Post Office to Addressee" service Mailing Label Number EL780371523US

Type a plus sign (+) inside this box [ ]

H 4304 PCT/US

DECLARATION

Page 2

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code §112.1 acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number *(if applicable)*
	PCT/EP00/08435	08/30/2000	

[ ] Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

[ ] Firm Name [ ] Customer Number or label

OR

[X] List Attorney(s) and/or agent(s) name and registration number below:

Name	Registration Number	Name	Registration Number
John E. Drach	32,891	Aaron R. Ettelman	42,516
Steven J. Trzaska	36,296	Henry E. Millson, Jr.	18,980

[ ] Additional attorney(s) and/or agent(s) named on a supplemental sheet attached hereto.

Please direct all correspondence to: [X] Customer Number or label **23657** OR [X] Fill in correspondence address below

Name	Aaron R. Ettelman				
Address					
Address					
City		State		ZIP	
Country		Telephone	610-278-4930	Fax	610-278-4971

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: [ ] A petition has been filed for this unsigned

Given Name	**Christine**	Middle Initial		Family Name	**Gaertner**	Suffix e.g. Jr.	
Inventor's Signature					Date	Febr. 26, 2002	
Residence: City	**Duesseldorf**	State		Country	**Germany**	Citizenship	**Germany**
Post Office Address	**Gotenstrasse 3**						
Post Office Address							
City	**40225 Duesseldorf**	State		Zip		Country	**Germany**
Applicant Authority							

[X] Additional inventors are being named on supplemental sheet(s) attached hereto

Type a plus sign (+) inside this box ☐

H 4304 PCT/US

DECLARATION

ADDITIONAL INVENTOR(S) Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name	Wilhelm	Middle Initial		Family Name	Stahl	Suffix e.g. Jr.	
Inventor's Signature	Stahl Wilhelm			Date	12.3.2002		
Residence: City	Duesseldorf	State		Country	Germany	Citizenship	Germany
Post Office Address	Luegallee 6						
Post Office Address							
City	40545 Duesseldorf	State		Zip		Country	Germany
Applicant Authority							

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name	Ulrike	Middle Initial		Family Name	Heinrich	Suffix e.g. Jr.	
Inventor's Signature				Date			
Residence: City	Wetter	State		Country	Germany	Citizenship	Germany
Post Office Address	Altarhof 6						
Post Office Address							
City	58300 Wetter	State		Zip		Country	Germany
Applicant Authority							

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature				Date			
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Applicant Authority							

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature				Date			
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Applicant Authority							

☐ Additional inventors are being named on supplemental sheet(s) attached hereto

Type a plus sign (+) inside this box ☐ H 4304 PCT/US

DECLARATION

ADDITIONAL INVENTOR(S) Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name	Wilhelm	Middle Initial		Family Name	Stahl	Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City	Duesseldorf	State		Country	Germany	Citizenship	Germany
Post Office Address	Luegallee 6						
Post Office Address							
City	40545 Duesseldorf	State		Zip		Country	Germany	Applicant Authority	

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

300

Given Name	Ulrike	Middle Initial		Family Name	Heinrich	Suffix e.g. Jr.	
Inventor's Signature	Ulrike Heinrich					Date	Feb. 28, 2002
Residence: City	Wetter	State		Country	Germany	Citizenship	Germany
Post Office Address	Altarhof 6						
Post Office Address							
City	58300 Wetter	State		Zip		Country	Germany	Applicant Authority	

DER

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country		Applicant Authority	

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country		Applicant Authority	

☐ Additional inventors are being named on supplemental sheet(s) attached hereto